U. S. PHARMACOPEIA
NATIONAL FORMULARY
SUPPLEMENT

10

PAGES 4741–5121
OFFICIAL
MAY 15, 1999

91 new monographs

Depressor substances test requirements eliminated from USP; Chapter <101> Depressor Substances Test deleted; Requirements, involving cats, deleted from 34 monographs

Botanicals—Cranberry; Milk Thistle; Saw Palmetto—4 NF monographs

Sunscreens—11 new USP monographs

Title changes to become official May 15, 1999
Several injectable dosage forms; Delayed-release terminology for 6 Tablets monographs

Revisions of <11> USP Reference Standards —Up-to-date cumulative list and label text

IMPORTANT!
Save Supplement 1 and all succeeding Supplements

USP 23–NF 18

Delete the following:

■**Depressor substances**—It meets the requirements of the *Depressor Substances Test* ⟨101⟩, the test dose being 1.0 mL per kg of a solution in sterile saline TS, containing 3.0 mg of dihydrostreptomycin per mL.■10

Bacterial endotoxins ⟨85⟩—It contains not more than 0.5 USP Endotoxin Unit per mg of dihydrostreptomycin.

Sterility ⟨71⟩—It meets the requirements when tested as directed in the section *Membrane Filtration Method* under *Test Procedures*.

pH ⟨791⟩: between 5.0 and 8.0.

Assay—

Assay preparation 1 (where it is represented as being in a single-dose container)—Withdraw all of the withdrawable contents of Injection, using a suitable hypodermic needle and syringe, and dilute quantitatively with water to obtain a solution containing a convenient quantity of dihydrostreptomycin in each mL.

Assay preparation 2 (where the label states the quantity of dihydrostreptomycin in a given volume of solution)—Dilute an accurately measured volume of Injection quantitatively with water to obtain a solution containing a convenient quantity of dihydrostreptomycin in each mL.

Procedure—Proceed as directed for the turbidimetric assay of dihydrostreptomycin under *Antibiotics—Microbial Assays* ⟨81⟩, using an accurately measured volume of *Assay preparation* diluted quantitatively with water to yield a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.■s

Diltiazem Hydrochloride Extended-Release Capsules

Add the following:

■**Labeling**—The labeling indicates the *Drug Release Test* with which the product complies.■s

Change to read:

■**Drug release** ⟨724⟩—

FOR PRODUCTS LABELED FOR DOSING EVERY 12 HOURS—

Test 1: If the product complies with this test, the labeling indicates that it meets USP *Drug Release Test 1*. Proceed as directed for *Extended-Release Articles—General Drug Release Standard* ⟨724⟩.

Medium: water; 900 mL.

Apparatus 2: 100 rpm.

Times: 3, 9, and 12 hours.

Procedure—Determine the amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 237 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Diltiazem Hydrochloride RS in the same *Medium*.

Tolerances—The percentages of the labeled amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved at the times specified conform to the *Acceptance Table* given.

Time (hours)	Amount dissolved
3	between 10% and 25%
9	between 45% and 85%
12	not less than 70%

Acceptance Table

Level	Number Tested	Criteria
L_1	6	No individual value lies outside each of the stated ranges, and no individual value is less than the stated amount at the final test time.
L_2	6	The average value of the 12 units ($L_1 + L_2$) lies within each of the stated ranges and is not less than the stated amount at the final test time. At 3 hours none of the units is outside the range of 10% to 35% of labeled content; at 9 hours none of the units is outside the range of 45% to 95% of labeled content; and at 12 hours none of the units is less than 65% of labeled content at the final test time.
L_3	12	The average value of the 24 units ($L_1 + L_2 + L_3$) lies within each of the stated ranges and is not less than the stated amount at the final test time. At 3 hours not more than 2 of the 24 units are outside the range of 10% to 35% of labeled content, and these two units must be within the range of 5% to 45% of labeled content; at 9 hours not more than 2 of 24 of the units are outside the range of 45% to 95% of labeled content, and these two units must be within the range of 35% to 100% of labeled content; at 12 hours not more than 2 of the 24 units are less than 65% of labeled content at the final test time, and these two units cannot be less than 60% of labeled content at the final test time.

■*Test 4:* If the product complies with this test, the labeling indicates that it meets USP *Drug Release Test 4*.

Medium, Apparatus, and *Procedure*—Proceed as directed under *Test 1*.

Times: 4, 8, 12, and 24 hours.

Tolerances—The percentages of the labeled amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved at the times specified conform to *Acceptance Table 1* under *Drug Release* ⟨724⟩.

Time (hours)	Amount dissolved
4	between 10% and 25%
8	between 35% and 60%
12	between 55% and 80%
24	not less than 80%

Test 5: If the product complies with this test, the labeling indicates that it meets USP *Drug Release Test 5*.

Medium: 0.05 *M* phosphate buffer, pH 7.2; 900 mL.

Apparatus 2: 50 rpm.

Procedure—Proceed as directed under *Test 1*.

Times: 1, 3, and 8 hours.

Tolerances—The percentages of the labeled amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved at the times specified conform to *Acceptance Table 1* under *Drug Release* ⟨724⟩.

Time (hours)	Amount dissolved
1	not more than 15%
3	between 45% and 70%
8	not less than 80%■s

FOR PRODUCTS LABELED FOR DOSING EVERY 24 HOURS—

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Drug Release Test 2*.

Medium, Apparatus, and *Procedure*—Proceed as directed under *Test 1*.

Times: 1, 4, 10, and 15 hours.

Tolerances—The percentages of the labeled amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved at the times specified conform to *Acceptance Table 1* under *Drug Release* ⟨724⟩.

Time (hours)	Amount dissolved
1	between 5% and 20%
4	between 30% and 50%
10	between 70% and 90%
15	not less than 80%

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Drug Release Test 3*.

Medium: 0.1 *N* hydrochloric acid; 900 mL.
Apparatus 2: 100 rpm.
Times: 6, 12, 18, 24, and 30 hours.
Procedure—Determine the amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 237 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Diltiazem Hydrochloride RS in the same medium.
Tolerances—The percentages of the labeled amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved at the times specified conform to *Acceptance Table 1* under *Drug Release* ⟨724⟩.

Time (hours)	Amount dissolved
6	between 20% and 45%
12	between 25% and 50%
18	between 35% and 70%
24	not less than 70%
30	not less than 85%

•*Test 6:* If the product complies with this test, the labeling indicates that it meets USP *Drug Release Test 6.*
Medium • and *Procedure*—Proceed as directed for *Test 1.*
•*Apparatus 1:* 100 rpm.•
Times: 2, 4, 8, 12, and 16 hours.
Tolerances—The percentages of the labeled amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved at the times specified conform to *Acceptance Table 1* under *Drug Release* ⟨724⟩.

Time (hours)	Amount dissolved
2	not more than 25%
4	between 25% and •50%••
•8	between 60% and 85%
12	not less than 70%
16	not less than 80%•

•*Test 7:* If the product complies with this test, the labeling indicates that it meets USP *Drug Release Test 7.*
Medium: pH 4.2 acetate buffer; 900 mL. Prepare the buffer employing the following method. Transfer 115 mL of acetic acid to a 10-liter volumetric flask, dilute with water to volume, and mix (Solution A). Transfer 165.4 g of anhydrous sodium acetate to a 10-liter volumetric flask, dilute with water to volume, and mix (Solution B). Mix 4410 mL of Solution A with 1590 mL of Solution B. Adjust, if necessary, with the addition of Solution A or Solution B to a pH of 4.2 ± 0.05.
Apparatus 2: 100 rpm.
Times: 1, 4, 10, and 15 hours.
Procedure—Determine the amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 237 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Diltiazem Hydrochloride RS in the same *Medium.*
Tolerances—The percentages of the labeled amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved at the times specified conform to *Acceptance Table 1* under *Drug Release* ⟨724⟩.

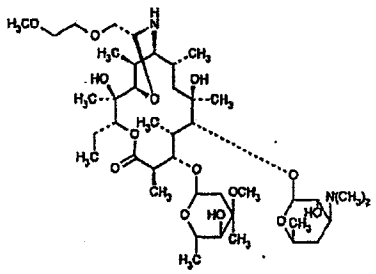
Time (hours)	Amount dissolved
1	not more than 10%
4	between 15% and 35%
10	between 65% and 85%
15	not less than 80%

Test 8: If the product complies with this test, the labeling indicates that it meets USP *Drug Release Test 8.*
Medium, Apparatus, and *Procedure*—Proceed as directed under *Test 1.*
Times: 1, 4, 10, and 15 hours.
Tolerances—The percentages of the labeled amount of $C_{22}H_{26}N_2O_4S \cdot HCl$ dissolved at the times specified conform to *Acceptance Table 1* under *Drug Release* ⟨724⟩.

Time (hours)	Amount dissolved
1	between 5% and 20%
4	between 30% and 50%
10	between 60% and 90%
•15	not less than 80%•

Add the following:

•Dirithromycin



$C_{42}H_{78}N_2O_{14}$ 835.09
Erythromycin, 9-deoxo-11-deoxy-9,11-[imino[2-(2-methoxyethoxy)ethylidene]oxy]-, [9*S*(*R*)]-.
(9*S*)-9-Deoxo-11-deoxy-9,11-[imino[(1*R*)-2-(2-methoxyethoxy)ethylidene]oxy]erythromycin
[*62013-04-1*].

» Dirithromycin contains not less than 96.0 percent and not more than 102.0 percent of $C_{42}H_{78}N_2O_{14}$, consisting of the 16*R*- and 16*S*-epimers, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers.
USP Reference standards ⟨11⟩—*USP Dirithromycin RS.*
Identification—
A: *Infrared Absorption* ⟨197K⟩.
B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay.*
Water, *Method I* ⟨921⟩: not more than 1.0%.
Heavy metals, *Method II* ⟨231⟩: 0.002%.
Limit of dirithromycin 16*S*-epimer—Using the chromatogram obtained in the test for *Chromatographic purity*, calculate the percentage of dirithromycin 16*S*-epimer in the portion of Dirithromycin taken by the formula:

$$1000(C/W)(r_E/r_S),$$

in which r_E is the response for dirithromycin 16*S*-epimer found in the chromatogram of the *Test solution;* and the other terms are as defined therein: not more than 1.5% of dirithromycin 16*S*-epimer is found.
Chromatographic purity—
Potassium phosphate buffer, Mobile phase, System suitability solution, Solvent, and *Chromatographic system*—Proceed as directed in the *Assay.*
Standard solution—Quantitatively dissolve an accurately weighed quantity of USP Dirithromycin RS in *Solvent* to obtain a solution having a known concentration of about 0.2 mg per mL.
Test solution—Transfer about 100 mg of Dirithromycin, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with *Solvent* to volume, and mix.
Procedure—[NOTE—Use peak areas where peak responses are indicated.] Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, and record the chromatograms for a period of time that is not less than three times the retention time of dirithromycin (16*R*-epimer). Calculate the percentage of each impurity found in the portion of Dirithromycin taken by the formula:

$$1000(C/W)(r_i/r_S),$$

in which C is the concentration, in mg per mL, of USP Dirithromycin RS in the *Standard solution; W* is the quantity, in mg, of Dirithromycin taken to prepare the *Test solution; r_i* is the response for each impurity found in the chromatogram of the *Test solution;*

between the top and bottom of the specimen, at a regular rate of 20 complete cycles per minute.

Congelation frequently may be induced by rubbing the inner walls of the test tube with the thermometer, or by introducing a small fragment of the previously congealed substance. Pronounced supercooling may cause deviation from the normal pattern of temperature changes. If the latter occurs, repeat the test, introducing small particles of the material under test in solid form at 1° intervals as the temperature approaches the expected congealing point.

Record the reading of the test tube thermometer every 30 seconds. Continue stirring only so long as the temperature is gradually falling, stopping when the temperature becomes constant or starts to rise slightly. Continue recording the temperature in the test tube every 30 seconds for at least 3 minutes after the temperature again begins to fall after remaining constant.

The average of not less than four consecutive readings that lie within a range of 0.2° constitutes the congealing temperature. These readings lie about a point of inflection or a maximum, in the temperature-time curve, that occurs after the temperature becomes constant or starts to rise and before it again begins to fall. The average to the nearest 0.1° is the congealing temperature.

⟨711⟩ DISSOLUTION

Change to read:

This test is provided to determine compliance with the dissolution requirements where stated in the individual monograph for a tablet or capsule dosage form. ■Of the types of apparatus described herein, use the one specified in the individual monograph.■ Where the label states that an article is enteric-coated, and a dissolution or disintegration test that does not specifically state that it is to be applied to enteric-coated articles is included in the individual monograph, the test for *Delayed-Release Articles* under *Drug Release* ⟨724⟩ is applied unless otherwise specified in the individual monograph. ■For hard or soft gelatin capsules and gelatin-coated tablets that do not conform to the *Dissolution* specification, repeat the test as follows. Where water or a medium with a pH of less than 6.8 is specified as the *Medium* in the individual monograph, the same *Medium* specified may be used with the addition of purified pepsin that results in an activity of 750,000 Units or less per 1000 mL. For media with a pH of 6.8 or greater, pancreatin can be added at not more than 0.05 g per 1000 mL.■

USP Reference Standards ⟨11⟩—*USP Prednisone Tablets RS* (*Dissolution Calibrator, Disintegrating*). *USP Salicylic Acid Tablets RS* (*Dissolution Calibrator, Nondisintegrating*).

Change to read:

Apparatus 1—The assembly consists of the following: a covered vessel made of glass or other inert, transparent material[1]; a motor; a metallic drive shaft; and a cylindrical basket. The vessel is partially immersed in a suitable water bath of any convenient size ■or placed in a heating jacket. The water bath or heating jacket■ permits holding the temperature inside the vessel at 37 ± 0.5° during the test and keeping the bath fluid in constant, smooth motion. No part of the assembly, including the environment in which the assembly is placed, contributes significant motion, agitation, or vibration beyond that due to the smoothly rotating stirring element. Apparatus that permits observation of the specimen and stirring element during the test is preferable. The vessel is cylindrical, with a hemispherical bottom ■and with one of the following dimensions and capacities: for a nominal capacity of 1 liter, the height is 160 mm to 210 mm and its inside diameter is 98 mm to 106 mm; for a nominal capacity of 2 liters, the height is 280 mm to 300 mm and its inside diameter is 98 mm to 106 mm; and for a nominal capacity of 4 liters, the height is 280 mm to 300 mm and its inside diameter is 145 mm to 155 mm.■ Its sides are flanged at the top. A fitted cover may be used to retard evaporation.[2] The shaft is positioned so that its axis is not more than 2 mm at any point from the vertical axis of the vessel and rotates smoothly and without significant wobble. A speed-regulating device is used that allows the shaft rotation speed to be selected and maintained at the rate specified in the individual monograph, within ±4%.

[1] The materials should not sorb, react, or interfere with the specimen being tested.

[2] If a cover is used, it provides sufficient openings to allow ready insertion of the thermometer and withdrawal of specimens.

Shaft and basket components of the stirring element are fabricated of stainless steel, type 316 or equivalent, to the specifications shown in Figure 1. Unless otherwise specified in the individual monograph, use 40-mesh cloth. A basket having a gold coating 0.0001 inch (2.5 µm) thick may be used. The dosage unit is placed in a dry basket at the beginning of each test. The distance between the inside bottom of the vessel and the basket is maintained at 25 ± 2 mm during the test.

Change to read:

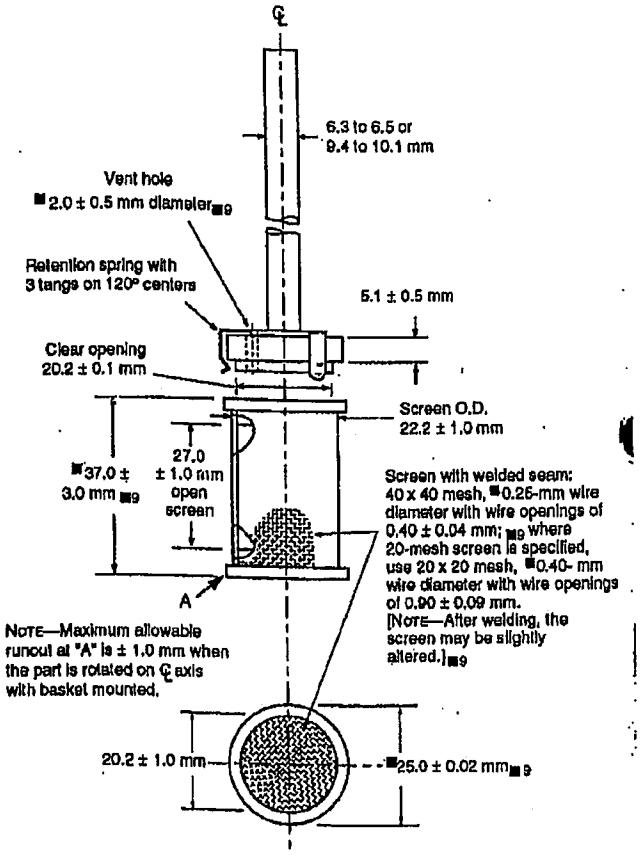


Fig. 1. Basket Stirring Element.

Change to read:

Apparatus 2—Use the assembly from *Apparatus 1*, except that a paddle formed from a blade and a shaft is used as the stirring element. The shaft is positioned so that its axis is not more than 2 mm at any point from the vertical axis of the vessel and rotates smoothly without significant wobble. ■The vertical center line of the blade passes through the axis of the shaft■ so that the bottom of the blade is flush with the bottom of the shaft. The paddle con-

forms to the specifications shown in Figure 2. The distance of 25 ± 2 mm between the blade and the inside bottom of the vessel is maintained during the test. The metallic ■or suitably inert, rigid■ blade and shaft comprise a single entity that may be coated with a suitable inert coating. The dosage unit is allowed to sink to the bottom of the vessel before rotation of the blade is started. A small, loose piece of nonreactive material such as not more than a few turns of wire helix may be attached to dosage units that would otherwise float. ■Other validated sinker devices may be used.■

Apparatus Suitability Test—Individually test 1 tablet of the *USP Dissolution Calibrator, Disintegrating Type* and 1 tablet of *USP Dissolution Calibrator, Nondisintegrating Type*, according to the operating conditions specified. The apparatus is suitable if the results obtained are within the acceptable range stated in the certificate for that calibrator in the apparatus tested.

Dissolution Medium—Use the solvent specified in the individual monograph. If the *Dissolution Medium* is a buffered solution, adjust the solution so that its pH is within 0.05 unit of the pH specified in the individual monograph. [NOTE—Dissolved gases can cause bubbles to form, which may change the results of the test. In such cases, dissolved gases should be removed prior to testing.[3]]

Time—Where a single time specification is given, the test may be concluded in a shorter period if the requirement for minimum amount dissolved is met. If two or more times are specified, specimens are to be withdrawn only at the stated times, within a tolerance of ±2%.

Change to read:

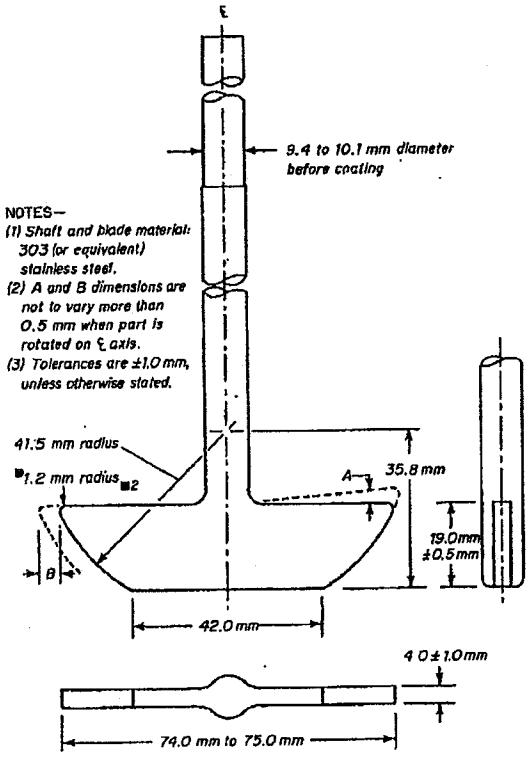


Fig. 2. Paddle Stirring Element.

Change to read:

[3] One method of deaeration is as follows: Heat the medium, while stirring gently, to about ■41°,■ immediately filter under vacuum using a filter having a porosity of 0.45 µm or less, with vigorous stirring, and continue stirring under vacuum for about 5 minutes. Other validated deaeration techniques for removal of dissolved gases may be used.

Change to read:

Procedure for Capsules, Uncoated Tablets, and Plain Coated Tablets—Place the stated volume of the *Dissolution Medium* ■(±1%)■, in the vessel of the apparatus specified in the individual monograph, assemble the apparatus, equilibrate the *Dissolution Medium* to 37 ± 0.5°, and remove the thermometer. Place 1 tablet or 1 capsule in the apparatus, taking care to exclude air bubbles from the surface of the dosage-form unit, and immediately operate the apparatus at the rate specified in the individual monograph. Within the time interval specified, or at each of the times stated, withdraw a specimen from a zone midway between the surface of the *Dissolution Medium* and the top of the rotating basket or blade, not less than 1 cm from the vessel wall. [NOTE—Replace the aliquots withdrawn for analysis with equal volumes of fresh *Dissolution Medium* at 37° or, where it can be shown that replacement of the medium is not necessary, correct for the volume change in the calculation. Keep the vessel covered for the duration of the test, and verify the temperature of the mixture under test at suitable times.] Perform the analysis as directed in the individual monograph.[4] Repeat the test with additional dosage form units.

■If automated equipment is used for sampling and the apparatus is modified, validation of the modified apparatus is needed to show that there is no change in the agitation characteristics of the test.■

Where capsule shells interfere with the analysis, remove the contents of not less than 6 capsules as completely as possible, and dissolve the empty capsule shells in the specified volume of *Dissolution Medium*. Perform the analysis as directed in the individual monograph. Make any necessary correction. Correction factors greater than 25% of the labeled content are unacceptable.

Change to read:

■**Procedure for a Pooled Sample for Capsules, Uncoated Tablets, and Plain Coated Tablets**—Use this procedure where *Procedure for a Pooled Sample* is specified in the individual monograph. Proceed as directed under *Procedure for Capsules, Uncoated Tablets, and Plain Coated Tablets*. Combine equal volumes of the filtered solutions of the six ■or twelve■ individual specimens withdrawn, and use the pooled sample as the test solution. Determine the average amount of the active ingredient dissolved in the pooled sample.■

Change to read:

Interpretation—

■*Unit Sample*—■ Unless otherwise specified in the individual monograph, the requirements are met if the quantities of active ingredient dissolved from the units tested conform to the accompanying Acceptance Table. Continue testing through the three stages unless the results conform at either S_1 or S_2. The quantity, Q, is the amount of dissolved active ingredient specified in the individual monograph, expressed as a percentage of the labeled content; ■ the 5%, ■15%, and 25%■ values in the Acceptance Table are percentages of the labeled content so that these values and Q are in the same terms.

Acceptance Table

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit is not less than Q + 5%.
S_2	6	Average of 12 units (S_1 + S_2) is equal to or greater than Q, and no unit is less than Q − 15%.
S_3	12	Average of 24 units (S_1 + S_2 + S_3) is equal to or greater than Q, not more than 2 units are less than Q − 15%, and no unit is less than Q − 25%.

■*Pooled Sample*—Unless otherwise specified in the individual monograph, the requirements are met if the quantities of active ingredient dissolved from the pooled sample conform to the accompanying Acceptance Table for a Pooled Sample. Continue testing through the three stages unless the results conform at either S_1 or S_2. The quantity, Q, is the amount of dissolved active ingredient

[4] If test specimens are filtered, use an inert filter that does not cause adsorption of the active ingredient or contain extractable substances that would interfere with the analysis.

specified in the individual monograph, expressed as a percentage of the labeled content.■S

Add the following:

■**Acceptance Table for a Pooled Sample.**

Stage	Number Tested	Acceptance Criteria
S_1	6	Average amount dissolved is not less than Q + 10%.
S_2	6	Average amount dissolved (S_1 + S_2) is equal to or greater than Q + 5%.
S_3	12	Average amount dissolved (S_1 + S_2 + S_3) is equal to or greater than Q.■S

⟨741⟩ MELTING RANGE OR TEMPERATURE

Change to read:

For Pharmacopeial purposes, the melting range or temperature of a solid is defined as those points of temperature within which, or the point at which, the solid coalesces and is completely melted, except as defined otherwise for *Classes II* and *III* below. Any apparatus or method capable of equal accuracy may be used. The accuracy should be checked ■at suitable intervals■10 by the use of one or more of the six USP Melting Point Reference Standards, preferably ■those that melt nearest the melting temperatures of the compounds being■10 tested (see *USP Reference Standards* ⟨11⟩).

Five procedures for the determination of melting range or temperature are given herein, varying in accordance with the nature of the substance. When no class is designated in the monograph, use the procedure for *Class Ia*.

The procedure known as the mixed-melting point determination, whereby the melting range of a solid under test is compared with that of an intimate mixture of equal parts of the solid and an authentic specimen of it, e.g., the corresponding USP Reference Standard, if available, may be used as a confirmatory identification test. Agreement of the observations on the original and the mixture constitutes reliable evidence of chemical identity.

Change to read:

■**Apparatus I**—An example of a suitable melting range *Apparatus I*■8 consists of a glass container for a bath of transparent fluid, a suitable stirring device, an accurate thermometer (see *Thermometers* ⟨21⟩),* and a controlled source of heat. The bath fluid is selected with a view to the temperature required, but light paraffin is used generally and certain liquid silicones are well adapted to the higher temperature ranges. The fluid is deep enough to permit immersion of the thermometer to its specified immersion depth so that the bulb is still about 2 cm above the bottom of the bath. The heat may be supplied by an open flame or electrically. The capillary tube is about 10 cm long and 0.8 to 1.2 mm in internal diameter with walls 0.2 to 0.3 mm in thickness.

Add the following:

■**Apparatus II**—An instrument may be used in the procedures for *Classes I, Ia,* and *Ib*. An example of a suitable melting range *Apparatus II* consists of a block of metal that may be heated at a controlled rate, its temperature being monitored by a sensor. The block accommodates the capillary tube containing the test substance and permits monitoring of the melting process, typically by means of a beam of light and a detector. The detector signal may be processed by a microcomputer to determine and display the melting point or range, or the detector signal may be plotted to allow visual estimation of the melting point or range.■8

Change to read:

Procedure for Class I, ■Apparatus I■10—Reduce the substance under test to a very fine powder, and, unless otherwise directed, render it anhydrous when it contains water of hydration by drying it at the temperature specified in the monograph, or, when the substance contains no water of hydration, dry it over a suitable desiccant for not less than 16 hours.

Charge a capillary glass tube, one end of which is sealed, with sufficient of the dry powder to form a column in the bottom of the tube 2.5 to 3.5 mm high when packed down as closely as possible by moderate tapping on a solid surface.

Heat the bath until the temperature is about 30° below the expected melting point. Remove the thermometer, and quickly attach the capillary tube to the thermometer by wetting both with a drop of the liquid of the bath or otherwise, and adjust its height so that the material in the capillary is level with the thermometer bulb. Replace the thermometer, and continue the heating, with constant stirring, sufficiently to cause the temperature to rise at a rate of about 3° per minute. When the temperature is about 3° below the lower limit of the expected melting range, reduce the heating so that the temperature rises at a rate of about 1° to 2° per minute. Continue heating until melting is complete.

The temperature at which the column of the substance under test is observed to collapse definitely against the side of the tube at any point is defined as the beginning of melting, and the temperature at which the test substance becomes liquid throughout is defined as the end of melting or the "melting point." The two temperatures fall within the limits of the melting range.

Change to read:

Procedure for Class Ia, ■Apparatus I■10—Prepare the test substance and charge the capillary as directed for *Class I, ■Apparatus I*.■10 Heat the bath until the temperature is about 10° below the expected melting point and is rising at a rate of 1 ± 0.5° per minute. Insert the capillary as directed under *Class I, ■Apparatus I*■10 when the temperature is about 5° below the lower limit of the expected melting range, and continue heating until melting is complete. Record the melting range as directed for *Class I, ■Apparatus I*.■10

Change to read:

Procedure for Class Ib, ■Apparatus I■8—Place the test substance in a closed container and cool to 10°, or lower, for at least 2 hours. Without previous powdering, charge the cooled material into the capillary tube as directed for *Class I, ■Apparatus I,*■10 then immediately place the charged tube in a vacuum desiccator and dry at a pressure not exceeding 20 mm of mercury for 3 hours. Immediately upon removal from the desiccator, fire-seal the open end of the tube, and as soon as practicable proceed with the determination of the melting range as follows: Heat the bath until a temperature 10 ± 1° below the expected melting range is reached, then introduce the charged tube, and heat at a rate of rise of 3 ± 0.5° per minute until melting is complete. Record the melting range as directed for *Class I, ■Apparatus I*.■10

If the particle size of the material is too large for the capillary, pre-cool the test substance as above directed, then with as little pressure as possible gently crush the particles to fit the capillary, and immediately charge the tube.

Add the following:

■**Procedure for Class I, Apparatus II**—Prepare the substance under test and charge the capillary tube as directed for *Class I, Apparatus I*. Operate the apparatus according to the manufacturer's instructions. Heat the block until the temperature is about 30° below the expected melting point. Insert the capillary tube into the heating block, and continue heating at a rate of temperature increase of about 1° to 2° per minute until melting is complete.

The temperature at which the detector signal first leaves its initial value is defined as the beginning of melting, and the temperature at which the detector signal reaches its final value is defined as the end of melting, or the *melting point*. The two temperatures fall within the limits of the melting range.

In the event of dispute, only the melting range or temperature obtained as directed for *Class I, Apparatus I*, is definitive.■8

Change to read:

Procedure for Class II—Carefully melt the material to be tested at as low a temperature as possible, and draw it into a capillary tube, which is left open at both ends, to a depth of about 10 mm. Cool the charged tube at 10°, or lower, for 24 hours, or in contact with ice for at least 2 hours. Then attach the tube to the thermometer by suitable means, adjust it in a water bath so that the upper edge of the material is 10 mm below the water level, and heat as directed for *Class I, ■Apparatus I*■10 except, within 5° of the expected melt-

* ASTM Method E77 deals with "Verification and Calibration of Liquid-in-glass Thermometers."

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